REMARKS

Reconsideration and withdrawal of the rejections of the application are requested in view of the amendments and remarks presented herein, which place the application into condition for allowance.

I. Status of claims and formal matters

Claims 1-18 were pending. Claims 6-18 have been canceled. Claims 1-5 have been amended and claims 19-20 have been added.

Support for the amended and added claims can be found throughout the specification as originally filed. With respect to claim 1, support can be found, for example, at page 3, lines 21-31 and the examples, e.g. Example 5. Support for claim 2 can be found, for example, in Example 1, page 11, lines 5-11. Support for claims 3-5 can be found, for example, at page 4, lines 5-9 and page 6, lines 3-17. Support for new claims 19 and 20 can be found, for example, in Example 5 and 6, respectively.

No new matter has been added by these amendment or new claims.

It is submitted that the claims are patentably distinct over the prior art and that these claims are and were in full compliance with the requirements of 35 USC § 112. The amendments of the claims and/or added claims are not made for the purpose of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112; but simply for clarification and to round out the scope of protection to which Applicants are entitled. Furthermore, it is explicitly stated that these amendments should not give rise to any estoppel, as they are not narrowing amendments.

The Examiner is thanked for informing Applicants of the requirement to submit a supplemental Information Disclosure Statement (IDS) with respect to the references cited at pages 23-26 of the specification. An IDS and Form PTO-1449 containing the references will be submitted shortly after the filing of this Response.

II. The rejection under 35 USC § 101, first paragraph, is overcome

The Office Action rejected claims 1-5 under 35 USC § 101 as allegedly being directed to non-statutory subject matter. In accordance with the Office Action's remarks, claim 1 has been amended to include the recitation "transgenic." Further, the recitation "disruption" has been substituted for "deficiency." Accordingly, it is believed that the rejection has been obviated.

Therefore, reconsideration and withdrawal of the rejection are respectfully requested.

III. The rejections under 35 USC § 112, first paragraph, are overcome

Claims 1-5 were rejected under 35 USC § 112, first paragraph, as allegedly lacking enablement. The Examiner states that the specification is enabling for a transgenic mouse comprising a disruption of DAP12 in its genome "wherein the mouse exhibits hypomyelination in the frontal lobe of the cerebrum and the thalamus." The Examiner also states, however, that the specification does not provide enablement for "a non-human animal model of oligodendrocyte development disorders, wherein the non-human animal comprises a deficiency in chromosomal DAP12 gene function and shows an oligodendrocyte development disorder."

Essentially, the Examiner appears to contend that the claimed invention is not enabled with respect to (a) a non-human animal, (b) any oligodendrocyte development disorder, and (c) the claimed neuropsychiatric disorders of the invention.

With respect to (a), the Examiner asserts that while the specification provides guidance on how to make a transgenic mouse having a disrupted DAP12 gene, the specification allegedly does not provide guidance on making other non-human animals and contends that the invention is limited to mouse. The claims are now directed to a transgenic mouse model.

With respect to (b), the Examiner asserts that while the specification provides guidance as to hypomyelinosis of the thalamus it does not disclose a role of DAP12 in "every and all aspects of oligodendrocyte development," for example differentiation of O-2A cells into oligodendrocytes or astrocytes. The claims as currently amended are directed to a transgenic mouse model of oligodendrocyte developmental disorders wherein the mouse exhibits hypomyelinosis of the thalamus. Accordingly, the oligodendrocyte developmental disorders of the invention relate to those transgenic mice exhibiting hypomyelinosis of the thalamus and do not encompass "every and all aspects of oligodendrocyte development."

With respect to (c), the Examiner contends that the specification is not enabling for Huntington's disease as it is not a disease that occurs from myelinogenesis. The Examiner cites to Geyer et al. as support for the statement that Huntington's disease is a neurodegenerative disorder and does not result from myelinogenesis. However, Geyer et al. teaches that humans with Huntington's disease can lead to abnormal sensorimotor gating. A phenotype of the presently claimed transgenic mice is that they are impaired in sensorimotor gating. The present invention could be a useful model for Huntington's disease as both relate to impairments in sensorimotor gating.

Accordingly, the presently claimed invention is enabled by the originally-filed specification with respect to (a), (b) and (c) above. Therefore, reconsideration and withdrawal of the rejections are respectfully requested.

IV. The rejections under 35 USC § 102 are overcome

Claims 1-5 were rejected under 35 USC § 102(a) as allegedly being anticipated by Bakker et al., 2000, Immunity, 13:345-353 (hereinafter "Bakker"). Claims 1-5 were rejected under 35 USC § 102(a) as allegedly being anticipated by Tomasello et al., 2000, Immunity, 13:355-364 (hereinafter "Tomasello"). The Office Action rejected claims 1-5 under 35 USC § 102(e) as allegedly being anticipated by Vivier et al., US publication No. 2004/0045041, which was filed September 20, 2000 and published March 4, 2004. These rejections are respectfully traversed. Moreover, none of the cited references, either alone or in combination, anticipate, teach or fairly suggest the presently claimed invention.

Chapter 2131 of the MPEP states in part that "[a] claim is anticipated only if **each and every element** set forth in the claim is found, **either expressly or inherently** described, in a single prior art reference. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)." For a proper anticipation rejection, the reference "must **clearly and unequivocally disclose** the claimed compound or direct those skilled in the art to the compound without any need for picking, choosing, and combining various disclosures not directly related to each other by the teachings of the cited reference." See *In re Arkley*, 455 F.2d 586, 587, 172 USPQ 524, 526 (CCPA 1972) (emphasis added).

Said another way, to show an anticipation under 35 USC § 102, a two-prong inquiry must be satisfied in order for such a rejection to stand. First, the prior art reference must contain **all** of the elements of the claimed invention. *See Lewmar Marine Inc. v. Barient Inc.*, 3 U.S.P.Q.2d 1766 (Fed. Cir. 1987). Second, the prior art must contain an enabling disclosure. *See Chester v. Miller*, 15 U.S.P.Q.2d 1333, 1336 (Fed. Cir. 1990). A reference contains an enabling disclosure if a person of ordinary skill in the art could have combined the description of the invention in the prior art reference with his own knowledge of the art to have placed himself in possession of the invention. *See In re Donohue*, 226 U.S.P.Q. 619, 621 (Fed. Cir. 1985).

Applying the law to the instant facts, none of the references relied upon in the Office Action meet the above legal standards. In particular, the reference cited in the Office Action do not teach each and every element of the claims either expressly or inherently. Further, none of

the references contain an enabling disclosure that would place the skilled person in possession of the invention.

The Office Action alleges that the DAP12-/- mice of Bakker, Tomasello and Vivier "are identical or substantially identical, or are produced by identical or substantially identical processes" and therefore inherently possess the characteristics of the claimed invention. Applicants respectfully disagree.

The Examiner is respectfully reminded of the law on inherency. While it is understood that the express, implicit and inherent disclosures of a reference may be relied upon in an anticipation rejection, the fact that a certain result or characteristic **may** occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic. *In re Rijckaert*, 9 F.3d 1531, 1534, 28 USPQ2d 1955, 1957 (Fed. Cir. 1993). "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is **necessarily present** in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may **not be established by probabilities or possibilities**. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999). Further, "[i]n relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." *Ex parte Levy,* 17 USPQ2d 1461, 1464 (Bd. Pat. App. & Inter. 1990) (emphasis in original).

Unlike any of the cited references, the presently claimed invention is directed to a transgenic mouse model of oligodendrocyte developmental disorders wherein the transgenic mouse comprises a disruption in chromosomal DAP12 gene function and **exhibits hypomyelinosis of the thalamus**. None of the cited reference teach or suggest or inherently provide for a transgenic mouse having a disruption in DAP12 gene function and which shows the hypomyelinosis phenotype. The nature of the DAP12 gene disruption of the present invention and that of the prior references are **different** and no where do the references show, demonstrate, detect, or inherently disclose that the affected mice of the prior references would exhibit the hypomyelinosis phenotype.

Bakker relates to a study to determine the physiological role of DAP12 receptor complexes in natural killer cells and myeloid cells, i.e. the role of certain cell surface receptors

that associate with DAP12. The study involves generating DAP12-deficient mice by targeted gene disruption followed by examining the mice for effects on natural killer cell function (examining the natural killer cell compartment and detecting for expression of various DAP12 associated receptors) and immune function (effect of challenge of MOG peptide to induce EAE). The DAP12 gene disruption is reportedly a deletion in exons 3 and 4 of DAP12. While Bakker characterizes certain physiological aspects of the resultant transgenic mice (DAP12-/-), the study does not at any point teach or suggest or disclose any effects on brain tissue, including whether there is or is not hypomyelinosis of the thalamus.

Similarly, Tomasello and Vivier, which overlap in authorship/inventorship and appear to disclose similar and overlapping results, purport to study the alterations of natural killer and dendritic cell subsets observed in DAP12-deficient mice. The references describe the preparation of KΔY75/KΔY75 mice, which apparently carry a mutation in the DAP12 gene such that the resultant protein product lacks the Y75 residue and wild-type C terminus amino acid, which according to Figure 1 appears only to affect exon 5. Like Bakker, neither Tomasello nor Vivier at any point teach or suggest or disclose any effects on brain tissue, including the presence or absence of hypomyelinosis of the thalamus.

As shown above, the mutations described by Bakker, Tomasello and Vivier are quite different from the specific mutations of the present invention. It is certainly well known, given the general unpredictability in the field of recombinant genetics, that different mutations in the same gene can result in very different phenotypes. A good example is the RET proto-oncogene. Germline mutations of RET lead to multiple endocrine neoplasia (MEN) type 2. The disease produced varies depending on where in the RET gene the germline mutation sits, so the phenotype may be MEN-2A, MEN-2B, or familial medullary thyroid cancer. See Eng C. et al. "The relationship between specific RET proto-oncogene mutations and disease phenotype in multiple endocrine neoplasia type 2 - International RET mutation consortium analysis," JAMA (1996) Nov. 20;276(19):1575-9 (submitted in the accompanying IDS). Accordingly, as the cited reference do not at any point disclose, teach or suggest a transgenic mouse having a disruption in DAP12 and which exhibit hypomyelinosis of the thalamus, it is **entirely unknown** as to whether the prior described mice would exhibit the required phenotype. To conclude otherwise is contrary to the established case law on inherency as outlined above.

Accordingly, neither Bakker, Tomasello and Vivier teach or suggest each and every

element of the present invention, either expressly or inherently. Therefore, reconsideration and withdrawal of the rejections are respectfully requested.

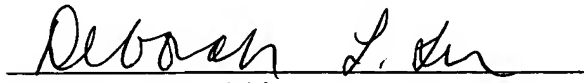
REQUEST FOR INTERVIEW

If any issue remains as an impediment to allowance, an interview, with supervisory review, is respectfully requested prior to issuance of any paper other than a Notice of Allowance. The Examiner is additionally respectfully requested to telephonically contact the undersigned to arrange a mutually convenient time and manner for the interview. The Examiner is also invited to telephonically contact the undersigned if there are any minor, formal issues that need resolving prior to issuance of a Notice of Allowance, with a view towards resolving such minor, formal issues via telephonic interview.

CONCLUSION

Reconsideration and withdrawal, or modification of the restriction requirement, and a prompt and favorable examination on the merits, is respectfully requested.

Respectfully submitted,
FROMMER LAWRENCE & HAUG LLP

By: 

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